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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/839,194	02/20/92	GORDON K	IG5-4.4

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EXAMINER	
CROUCH, D	
ART UNIT	PAPER NUMBER
1632	25

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Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 07/839,194	Applicant(s) Gordon et al.
	Examiner Deborah Crouch	Group Art Unit 1632

☒ Responsive to communication(s) filed on *August 11, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three (3)* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-3, 5-9, 11, 16, 17, 19-22, and 24-29* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3, 5-9, 11, 16, 17, 19-22, and 24-29* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Applicant's arguments filed August 11, 2000 in paper no. 24 have been fully considered but they are not persuasive. The amendment has been entered.

The claims as filed used improper numbering. The examiner has renumbered the claims of record to correspond with the claims of previously of record. Please note that an error in claim numbering occurred in the amendment filed December 27, 1999, as noted in the previous office action. Applicant requested entry of new claims 12-25. However, the next new claim numbers available to applicant were numbers 16-29, as claims 12-15 had been canceled with the amendment filed February 20, 1992. Thus the claim numbers were changed by the examiner under 37 U.S.C. 1.126. In the amendment filed August 11, 2000, applicant mis-numbered the claims by numbering claim 15 by your 12/27/99 amendment as claim 16. Thus the claims beginning with 16 filed 8/11/00 are off by one. The last claim should be claim 25 by your 12/27/00 amendment. The following is the number status of the claims in this order 12/27/99 amendment-8/11/00 amendment-examiner corrected number: 1-9 and 11 are all proper; 12=12=16; 13=13=17; 16=15=19; 17=16=20;18=17=21;19=18=22; 21=20=24; 22=21=25; 23=22=26; 23=24=17; 24=25=28 and 26=25=29. However, and this is critical, in an eye to comparison of the claims, applicant did not cancel claim 20 but claim 19, using the claim numbering of the 12/27/00 amendment. This error occurred because applicant mis-numbered the claims beginning with claim 16. Instead of requesting the claims 4, 14 and 20 be canceled, applicant meant claims 4,18 and 23 to be canceled. The correct claims of record and examined in this office action are: 1,2,5-9,11,16,17,19-22 and 24-29. This is very confusing. Applicant can contact the examiner for further explanation of the numbering and the numbering errors.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1,5-9,11,16,17,19-22 and 24-29 remain provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1,3-9,11 and 16-29 of copending Application No. 08/927,936. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 2 remains provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,2,4-9,11 and 16-29 of copending Application No. 08/927,936 for reasons of record.

Claims 1,2,5-9,11,16,19-21 and 24-29 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 24 of copending Application No. 08/246,259 for reasons of record.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Applicant has stated that these rejections will be addressed when the claims are found to be allowable.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,2,5-9,11,16,17,19-22 and 24-29 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The specification provides only a description of one mammalian serum milk protein promoter, and that is the WAP promoter. There is no description of any other WAP promoter or other mammalian milk serum protein promoter such that at the time of filing, 1986, it is evident that applicant had possession for the breadth of the claimed invention. Furthermore, the disclosure does not describe mammalian serum milk promoters for their breadth such that their structure could be envision by the skilled artisan at the time of filing. Thus, applicant is given a scope of written description to DNA constructs containing a gene encoding a protein, said gene being under transcriptional control of a WAP promoter.

Applicant's arguments are persuasive for the genus WAP promoters.

The Written Description Guidelines argued by the Examiner are those published in December 1999 (Fed. Reg., Vol. 64, No. 244, Tuesday, December 21, 1999, pages 71427-71440).

Applicant argues that the genus of milk protein promoters was well characterized and defined in the art at the time of filing. Applicant argues that five references published prior to the filing date identify the 3' and 5' regulatory regions, identify characteristic 5' regulatory structures and provide a significant amount of DNA sequence for the promoter regions of each of α-lactalbumin (Qasba et al, exhibit A), α-casein (Yu-Lee et al, exhibit C), β-casein (Jones et al, exhibit E) and γ-casein (Yu-Lee and Rosen, exhibit F). Applicant argues that the level of skill in the art with regard to the manipulation of eukaryotic promoters, and notably cell and tissue specific promoters, was routine in the art at the time of filing. Applicant argues that it was routine for one of skill in the art to pick a region and combine it with other elements of the claims. Applicant cites Ciliberto et al (Exhibit G) as identifying a promoter to regulate a heterologous gene. Applicant argues that Ciliberto et al teaches 133 of 1200 bases, and that the 133 bases were sufficient to provide expression. Applicant further argues that Campbell et al noted the presence of 105 eukaryotic 5' flanking sequences in GenBank™. Thus applicant argues that it was routine in the art to

obtain mammalian promoters and to couple them to heterologous genes. Applicant further cites Walker et al (Exhibit II), Krumlauf et al (Exhibit I), Ott et al (Exhibit J), Ornitz et al (Exhibit K), Palmiter et al (Exhibit L), Magram et al (Exhibit M), Ishii et al (Exhibit N), Melton et al (Exhibit O), Reynolds et al (Exhibit P) and Valerio et al (Exhibit Q) as evidence of the routine nature of isolating promoter sequences and expressing a heterologous gene by the promoters. Applicant argues that possession of the genus "milk protein promoters" is demonstrated in a variety of ways: that the references cited above provide for significant 5' regulatory regions for each of two types of milk protein promoters other than WAP, α-lactalbumin and the caseins (α, β and γ). Applicant argues that the naming of the milk protein promoter provides an identifying characteristic, and that given the state of the art at the time of filing, the naming of an art-known promoter is sufficient written description. Applicant argues that the knowledge of milk protein promoters, including partial sequence information, was well developed in the art. Applicant argues that the Guidelines for Written Description recognize that the level of description needed depends on how much was known in the art about the subject matter. Applicant argues that the Guidelines instruct the examiner to determine whether the specification discloses other relevant identifying characteristics sufficient to describe the claimed invention in such full clear, concise and exact terms so that the skilled artisan was in possession of the claimed invention. Applicant argues that the Guidelines explicitly require that printed publications should be relied upon to determine the level of knowledge and skill in the art. Applicant points to the above discussed exhibits. Applicant argues as structural information, including sequence information, on milk promoters was known in the art at the time of filing.

Applicant argues that claims in the instant matter, unlike those in Amgen, Fiers and U.C. v. Lilly are not drawn to novel gene sequence defined only by function in the specification and not known in the art. Applicant argues that the essential characteristics of the inventions in Amgen, Fiers and U.C. v. Lilly was the determination of a nucleotide sequence not known in the art. With regard to Amgen, applicant argues that the court considered written description of a previously uncharacterized gene. Applicant argues that there was no other information in the court cases referenced, other than the information disclosed in the specification, for an artisan to rely on to determine if the inventor was in possession and to

be able to distinguish the invention from other materials. In contrast applicant argues the instant invention elements were present in the art at the time of filing. Applicant argues that their invention, a vector comprising known elements is quite unlike the novel gene sequence in Amgen. Applicant argues that in Amgen the invention was knowledge of base-by-base sequence, whereas such knowledge is irrelevant in the instant case. Applicant argues that the holding in Amgen is specifically limited to a gene.

Applicant argues that in Fiers v. Revel the applicants attempted to establish conception of a novel gene by providing a protocol for isolating the gene, but no sequence data. Applicant argues that the court in Fiers v. Revel that conception of a DNA requires a definition more that by its functional utility. Applicant argues that the recitation of the promoter, where the promoter is known and well characterized in the art is far more than mere recitation of the name of an unsequenced gene.

With regards to U.C. v. Lilly, applicant argues the court in Lilly stated that the name of a cDNA is not itself a written description of that DNA as it conveys no distinguishing information concerning its identity. Applicant argues in the instant case, the name of the promoter does convey distinguishing information concerning its identity. Applicant argues that the claim element was known in the art.

Applicant argues that the specification satisfied the written description requirement for the species claims to α-lactalbumin (claims 17 and 22, as renumbered according to page 2 of this office action). Applicant refers Qasba et al and the discussion of this reference. Applicant argues that the specification provides a written description for the genus of milk protein promoters, claims 1 and 19, as renumbered above. Applicant argues that a written description for α-lactalbumin is provided for by naming the promoter. With regard to the genus "milk promoters" applicant argues that the genus is very small, and thus relatively fewer species will describe the genus. Applicant argues that all the promoters share common canonical structures. Applicant further argues that the specification provides written description for the WAP promoter via the discussion at pages 10 and 12 of the specification as well as figures 1-5 and in view of Campbell et al,, the α-lactalbumin promoter via identification of the promoter by its art recognized name, and Qasba et al, which applicant argues characterizes the α-lactalbumin promoters and the casein promoters via the specification disclosing that the casein promoters should be used, and in view

of Yu-Lee et al, Jones et al and Yu-Lee and Rosen. Applicant argues that the Written Description Guidelines provide that the written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species. Applicant argues that the instant specification specifically describes both the WAP promoter and the α-lactalbumin promoter. Applicant argues that written description of 2 promoters out of seven is sufficient for written description of the genus given the fact that the promoters were in the art, and that methods for using and testing promoters were enabled by the specification. With regards to casein promoters, applicant argues that they did not explicitly name the casein promoters but taught the use of the genus casein promoters in the instant invention. Applicant argues that by naming the genus, the inventors were in possession of the genus casein promoters. Applicant argues that U.C. v. Lilly supports the view that there is not just one way to describe a genus. Applicant argues that for WAP and α-casein, promoters for more than one species were known. In this regard, applicant argues that for claims 12 and 21, renumbered as indicated above, two of the genus milk serum promoters, WAP and α-lactalbumin, are described.

The fundamental issue here is whether or not the specification in view of its stating the name of particular milk protein gene promoters or the genus name for milk protein gene promoters, and in view of the art teaching the genomic sequences, including 5' flanking regions, of milk protein genes provides evidence of possession of the claimed subject matter for its entire breadth. All of this is analyzed in view of the Written Description Guidelines mentioned above.

Qasba et al (exhibit A), Yu-Lee et al (exhibit C), Jones et al (exhibit E) and Yu-Lee and Rosen (exhibit F) teach the genomic sequence and structure for, respectively, α-lactalbumin, α-casein, β-casein and γ-casein. While each references teaches the presence of putative TATA boxes and CAAT boxes, the references never disclose the complete 5' structure that comprises the various milk protein promoter regions. There obviously is more to identifying a promoter than the presence of regions that resemble TATA box or CAAT boxes, as all promoters, even prokaryotic promoters, have these sequences. However, the claims require milk protein promoters. These are promoters that function only in the mammary gland, and have some special structural or sequence that affords them this designation. Thus more structure is

needed that TATA boxes and CAAT boxes to promoter the mammary gland location of expression as dictated by the claim, and indicated as necessary in the specification to make transgenic non-human mammals expression a heterologous protein in their milk. None of the references provided by applicant teach the location of any sequence or structure within the 5' flanking region for genes encoding α-lactalbumin, α-casein, β-casein and γ-casein that impart mammary gland specific expression. Thus, the references of Qasba et al, Yu-Lee et al, Jones et al and Yu-Lee and Rosen do not provide a written description for mammalian milk protein promoter sequences as broadly claimed. Furthermore, as discussed above, the references themselves do not state that they have taught promoter sequences. Qasba et al compare the sequence of the 5' flanking regions of rat α-lactalbumin and chicken lysozyme genes, and disclose the sequence of a rat α-lactalbumin gene (page 378). However, Qasba et al provide no guidance on those portions of the 5' flanking region which have promoter activity. Qasba et al state that the sequences found in the 5' flanking region are similar too, but not the same as consensus sequences found at initiation sites of other genes and not the same as consensus sequences for progesterone receptor recognition site of the ovalbumin gene (page 379, col. 2, parag. 1). Jones et al discuss the fine structure mapping of the rat β-casein gene, and propose sites of expression regulatory sequences, this is not considered enabling as no such promoter sequences were analyzed for such regulatory activity (page 7043, col. 2, parag. 1 and 2). These regions are referred to by Jones et al as "candidates for regulatory elements". Yu-Lee et al (1983) analyzes the rat γ-casein gene much as Jones et al did for the rat β-casein gene. Yu-Lee et al (1983) does not teach promoter sequences, but only points to proposed sites within the 5' flanking region of the γ-casein gene that may be promoter regions (page 10798, parag. 1 to page 10799, line 7). Yu-Lee et al (1986) states that a "possible Goldberg-Hogness box" (the TATA box) is present in the 5' flanking sequence of the rat γ-casein gene. Again, all the references do at most is point to structures and sequences common to all promoters, and not to point to structures that would make the promoter a mammary gland promoter or a milk protein promoter. Thus the art at the time of filing provides no teachings that indicate a general possession of milk protein promoters.

It would also appear that applicant is inserting standards for enablement into written description. The routineness of isolating promoter sequences is not at issue in this particular rejection. The factors set forth in *In re Wands* are not relevant to a written description rejection. None of the court decisions upon which the Written Description Guidelines are based state such. The issue is whether or not the skilled artisan would know that applicant, at the time of filing, had possession of the claimed invention for its breadth. The issue at hand in this rejection is whether applicant had possession of the structure or sequence of mammalian milk protein promoter sequences for the breadth claimed. The routineness of isolating such promoter sequences is not germane. The routineness of promoter isolation and identification at the time of filing is discussed below in the enablement rejection. In addition, the cited references of Ciliberto et al, Walker et al, Krumlauf et al, Ott et al, Ornitz et al, Palmiter et al, Magram et al, Ishii et al, Melton et al, Reynolds et al and Valerio et al do not teach anything regarding structures that cause the 5' flanking region of a milk protein gene to impart mammary gland specificity or that make the promoter a milk protein promoter rather than an insulin promoter. It is important at this point to realized that like the insulin gene promoter, which only expresses in pancreatic cells, the milk protein gene promoter is similarly characterized. There are special features of the milk protein gene promoter that make it a milk protein gene promoter. Without knowledge of the structure that makes a mammalian milk protein promoter a mammalian milk protein promoter, applicant would not have been seen by the skilled artisan at the time of filing as having possession of this category of promoters. These references further establish the knowledge in the art at the time of filing, and they do not establish knowledge of all structures and/or sequences required to make a mammalian milk protein promoter. The artisan would not have been able glean such knowledge from the art. No milk protein promoter identifying structural features were either disclosed in the specification nor known in the art at the time of filing. If these structures are not important to the invention, then, any promoter would suffice, and applicant's claim to milk protein promoters really would mean any promoter. As this is not applicant's intention, then the structural features of the milk protein promoter region that provide the function of being a milk protein promoter are critical to the invention, and thus are germane to written description of the invention. Contrary to applicant's assertion, the

examiner can find no bases in the specification or the art for knowledge of structures and/or sequences that landmark mammalian milk protein promoters. This discussion amounts to a full consideration of the state of the art at the time of filing as required by the Written Description Guidelines.

The written description rejection is a relevant rejection to the claims as milk protein promoters are an essential, critical feature to the claimed invention. As such, milk protein promoters must meet the written description requirement under 35 U.S.C. 112. The Guidelines support this in stating "the claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Fed. Reg., Vol. 64, No. 244, December 21, 1999, page 71434, col. 3, lines 7-12). Thus, as the claimed DNA constructs comprise milk protein promoters, it is proper to analyze the construct elements for compliance with written description. The Guidelines make no stipulation that only novel DNA sequences are to be so queried. Further, the holdings of Amgen, Fiers v. Revel and U.C. v. Lilly are applicable as there is no dicta or other guidance in these decisions that the holding therein are on to be used on claims to novel DNA sequences only. While the specific issues at hand may be somewhat different, the holding can be more generally applied. It is noteworthy that the courts have stated that structure is what is needed to satisfy the written description portion of 35 U.S.C. 112, first paragraph. Further, while Amgen, Fiers v. Revel and U.C. v. Lilly are specifically at issue with a previously unknown DNA sequence, the instant issue is very similar as the specific sequence or structure of the milk protein promoters was not known in the art at the time of filing, as discussed above. With respect to Amgen, while it is true that the 5' flanking regions for α-lactalbumin, α-casein, β-casein and γ-casein genes were known in the art at the time of filing, the relevant structure or sequence that makes these regions specific for expression of WAP, lactalbumin, lactoglobulin or casein were not known, were not taught in the cited references and not disclosed in the specification. With respect to Fiers and Lilly, the name of a milk protein promoter, or any promoter for that matter, does not describe in any fashion its structure. The name on proscribes a function, and function does not provide written description without structure. While Lilly may state other means can be used to describe a DNA sequence other than base pair order, Lilly did not offer such and applicant has failed to adequately

describe by another means, and the name is such an non-adequate means. Further, the decision as to the milk protein promoters being a genus is arbitrary on the part of applicant. An equally compelling argument can be made that each milk protein promoter class forms its own genus, and the species of the genus are like milk protein promoters from other species of mammal. Thus, under this analysis, the WAP protein promoter would be a genus, and the species would be an ovine WAP promoter, a bovine WAP promoter and so on. This in fact makes better analysis as each milk protein promoter is patentably distinct as knowledge of one milk protein promoter such as WAP neither anticipates or makes obvious a casein promoter because the promoters are distinct in nucleotide sequence, and other that the 5' flanking location of the promoter and the canonical TATA box and CAAT box, it is not clear how the different milk protein promoters are structurally similar. Therefore, written description of a WAP promoter does not provide written description of any other promoter than of the WAP genus. Essentially, under this reasoning, WAP only provides structure for WAP and not for β-casein as an example. Further, the fact that the number of milk protein promoters is not relevant given that they are of different sequence, and the sequences or structures that make them milk protein promoter, or a specific milk protein promoter is not known. When so much information was lacking at the time of filing about landmark features or canonical features of milk protein promoters, the number is not relevant. As stated above, at the time of filing neither the art nor the specification taught the sequence or structures that imbued mammary gland specificity, or which sequences other than TATA or CAAT boxes were needed to be a promoter. In deed, one could link a TATA box or CAAT box to a DNA sequence and that alone would not be sufficient for expression of the DNA sequence. It is these other structures for expression that are lacking in the art and specification at the time of filing, and thus induce the institution of a written description rejection. In this regard, it is unclear if applicant has provided sufficient guidance with regards to the genus of milk protein promoters.

With regard to the specific remarks made by the examiner in the previous office action, applicant argues that the court did not limit written description to disclosing a DNA sequence. Applicant argues that the Guidelines emphasize a case by case inquiry. Applicant argues that the examiner is attempting to

apply the most narrow holding in these cases which follow Amgen to a very different set of claims and a very different invention. It is noted that applicant has argued that the instant invention is different from those of Amgen, Fiers and Lilly in that they do not teach or claim a novel DNA sequence. Applicant argues that the examiner has not given sufficient weight to the concept that the level of knowledge in the art affects the level of disclosure needed. Applicant also argues, that, contrary to the examiner's statements in the previous office action, the physical structure of the promoter is needed but not the sequence and certainly not the entire sequence. Applicant argues that the sequence is not claimed. Applicant argues that the art at the time of filing teaches the structure. Applicant argues that the examiner is incorrect in stating that there is no physical description of promoters in the art.

Many of these arguments are answered above. In summary, the holds of Amgen, Fiers and Lilly is quite appropriate and are part of the Written Description Guidelines. Further, the holdings in court decisions are frequently applied broadly to cases with different fact patterns. If this were not the case, then the holding of In re Wands would only apply to cases where monoclonal antibodies were made. The essence here is structure, as opposed to absolute sequence. However, when the discussion concerns promoter sequences, DNA sequence is at least part of the total equation as it provides the structure. Thus, as the cited case law discusses DNA sequences in terms of structure, they are clearly applicable to more than novel genes. Thus, as stated above, absent teachings either in the art at the time of filing or the specification of structures in the 5' flanking sequences of the α-lactalbumin, α-casein, β-casein and γ-casein genes that make the promoters mammary gland specific or make the promoters behave as expression regulatory sequences, the claims lack written description for their entire breadth.

Applicant's arguments are persuasive to overcome the rejection made under 35 U.S.C. 112, first paragraph, as lacking enablement has been overcome. Between the specification's teaching of isolating the WAP 5' promoter sequence and the teachings of the art of the isolation and identifying multiple promoter sequences, some of which are tissue specific, it would not have required undue experimentation under the meaning established in *In re Wands*.

○

Applicant's amendments to the claims has overcome the rejection made in the previous office action under 35 U.S.C. 112, second paragraph.

The claims are free of the prior art. At the time of filing, the prior art did not teach or suggest a DNA construct containing a gene encoding a protein where expression of the gene is regulated by a mammalian milk serum protein promoter, where the promoter does not naturally regulate expression of the gene, and the construct further comprising a DNA sequence encoding a signal peptide.

U.S. Patents 5,476,995; 5366,894 and 5,322,777 are cited as of interest.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126. The examiner's SPE is Karen Hauda, whose telephone number is (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Art Unit Patent Analyst, Kay Pinkney, whose telephone number is (703) 305-3553.

The fax number is (703) 308-4242.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

Dr. D. Crouch
January 28, 2001